Understanding Major Depression in a Digital Environment

Pablo Ruisoto Palomera
Department of Basic Psychology, Psychobiology and Methodology of Behavioral Science
University of Salamanca, Spain
Email: ruisoto@usal.es

Juan A. Juanes Méndez
Department of Human Anatomy, Faculty of Medicine, University of Salamanca, Spain
Email: jajm@usal.es

María A. Velasco Marcos
Tejares Health Centre, Salamanca, Spain
Email: mauxi.velasco@comsalamanca.es

Israel Contador Castillo
Department of Basic Psychology, Psychobiology and Methodology of Behavioral Science
University of Salamanca, Spain
Email: icontador@usal.es

Alberto Prats Galino
Laboratory of Surgical Neuroanatomy, Faculty of Medicine, University of Barcelona, Spain
Email: aprats@ub.edu

The most recent neuroimaging studies offer new possibilities to learn the neurobiological basis of depressive disorders. This paper illustrates an interactive visual tool, based on Information and Communication Tech–nologies (ICT), to study the morphological and metabolic changes of brain structures in a patient with unipolar depression. In particular, this application provides a comprehensive representation of structures and neurotransmission changes involved in the pharmacological treatment of major depressive disorders. The ICT tool may be helpful to learn complex brain changes associated with depression. Some advantages of this approach in relation to conventional techniques are discussed.

Keywords: *major depression; neurobiology; neuroanatomy; three-dimensional visualization; educational software*

ACM Classifications: *H 1.2. User/Machine Systems; I.4. Image Processing and Computer Vision; J.3. Life and Medical Sciences; J.4. Social and Behavioral Sciences; K.3.1. Computer Uses in Education*

1. Introduction

The interest for neuroimaging studies in major depressive disorder (MDD) has increased during the last decade (Greden, 2011). Most of them apply conventional techniques (e.g., Magnetic Resonance Imaging, MRI or Single Photon Emission Tomography, SPECT) to study morphological and metabolic changes associated with MDD (Kimbrell *et al*, 2002; Koolschijn *et al*, 2009; Lorenzetti

Corresponding author: Dr Pablo Ruisoto, Department of Basic Psychology, Psychobiology and Methodology of Behavioral Science, Faculty of Psychology, ES-37005, University of Salamanca, Spain. Email: ruisoto@usal.es

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et al, 2009; Pol and Kahn, 2009; Savitz and Dreets, 2009). However, understanding the brain with conventional techniques, which rely on cross-sectional images, requires big efforts in terms of cognitive resources (Sweller, 1998). Hence, this factor has a negative effect on learning outcomes (Pass *et al*, 2003; Clark *et al*, 2006; Clark and Mayer, 2007). Nonetheless, it has been pointed out that three-dimensional embedded models enhance the performance of neuroanatomy students in comparison with those based on cross-sectional images (Ruisoto *et al*, 2011; Ruisoto *et al*, 2012).

Information and communication technology (ICT) tools offer new opportunities to facilitate teaching and learning neuroanatomy processes in clinical settings (Zinchuk *et al*, 2010). Some recommendations have been done to improve ICT tools oriented towards teaching neuronatomy, for instance, the integration of contents in a multimedia-interactive application (Paas *et al*, 2004; Paas *et al*, 2005; Novinski *et al*, 2009; Kirschner et al, 2011). Moreover, the organization of neuronatomical contents in simple graphical interfaces (e.g., icons) promotes a sense of control and more interaction with the application (Benbasat and Todd, 1993; Mordecki, 2007). The last aim of these factors would be to facititate both teaching and learning processes, but the integration of these type of resources for studying neuroanatomy is scarce.

The main objective of this paper is to show a visual and interactive ICT tool to study the neuro–biological basis of depression and other related mental disorders. In addition, we analysed the satisfaction in a sample of students who completed a period of neuroanatomy training with the application. The advantages of these techniques to study neuroanatomy and other neurobiological processes, in comparison with conventional techniques (e.g., cross-sectional images obtained from MRI), are reported in the discussion section.

2. Methods

MRI and SPECT images were acquired from a 45 year old male who was diagnosed with unipolar major depressive disorder according to DSM-IV-TR criteria (American Psychiatric Association, 2000). The patient signed an informed consent to participate in the study. Following the principles established in the Declaration of Helsinki, this study was approved by the local ethics committee. All images were acquired from the Clinical Hospital of Barcelona, Spain.

2.1 Material and Design

2.1.1. Acquisition of Images

A Magnetic Resonance unit (Philips Intera Medical Systems; 1.5 Tesla) was used for the acquisition of morphological brain images, whereas a Siemens Orbiter-Nco SPECT Gamma Camera was used for the registration of metabolic activity.

2.1.2. Creation of Three-dimensional Models and Co-registered Multimodal Images

Volumetric generation from two-dimensional MRI was done by Amira Version 5.3TM Visage Imaging. The creation of three dimensional models required two steps: 1) bilateral segmentation of the regions of interest (ROIs) for the brain structures from two-dimensional MRI sections; 2) creation of intermediate polygonal surface representations (i.e. mesh models) of the brain structures, considering the convergence of the ROIs, which were previously segmented.

Co-registration consisted of unifying information in data sets from the two image modalities (MRI & SPECT), that were obtained using craneometric landmarks as parameters with the same angle of acquisition. Position and orientation of both images was aligned and adjusted to maximize mutual information. As a result, the integration of three-dimensional models generated from morphological MRI imaging into functional SPECT imaging was possible.

2.1.3. Development of the Graphical User Interface and Animations

The development of the graphical user interface was made using programming language of objects Visual C++, generating two files: a workspace file (with .wsp extension) and a standard makefile (with extension .mak). Microsoft Windows APIs, DirectX and Microsoft.NET Framework tech–nology was also used. Aditionally, high quality digital graphical animations were created using Macromedia FlashTM to optimize quality/weight file value and ActionScript to incorporate interactivity to the tool.

The application was developed for Microsoft WindowsTM platforms. The recommended hardware and software requirements for its visualization are a 1028 x 800 pixel screen with a 1GB or higher video card, a 1,2GHz or higher processor, 1GB of RAM memory, 2GB of free memory space in the hard drive and CD-ROM.

2.1.4. Assessment of Satisfaction

Thirty-five voluntary medical students at the local university (23 females and 12 males) took part in the study to assess the satisfaction and perceived usefulness of this application. Mean age was 24.8±1.4 years old (range: 23–31). After 15 minutes of interaction with the tool, students performed an online Likert type scale composed of two items (range: 1–5) according to the following cate–gories: 1 "strongly disagree", 2 "partially or somewhat agree", 3 "neither agree nor disagree", 4 "partially or somewhat disagree", 5 "strongly agree".

3. Results

This application was developed for training purposes of neuroscience students. The viewer included the following elements: 1) three-dimensional models for brain structures related to major depression such as hippocampus, amygdala, corpus striatum, 2) functional SPECT images, 3) complementary information about mechanisms involved in the pharmacological treatment of major depression. Graphic controls were incorporated in the interaction with 3D models and plane cuts (Figure 1 *on following page*).

3.1. Visualization and Interactivity Features for Three-dimensional Models

Figure 1 shows the graphic control to regulate 3D model visualization (upper right). As shown above, 3D neuroanatomical models were organized with a hierarchical structure. Each model, which can be activated independently, is displayed with a simple mouse click on text/icons within the graphic control. A brief detailed text description is visible when placing the cursor over one of these icons. The following options allow interaction with the models: a) Selection. It is possible to select a particular 3D model corresponding to a specific brain structure clicking on it. At this point, the hierarchy level is open. b) Texts. Scientific and technical information of brain structures is available clicking on the option "text". c) Rotation movements. Any displayed view can be rotated keeping the left mouse button pressed and moving the cursor simultaneously. d) Translation movements. Users should press the mouse buttons and move the cursor at the same time. e) Zoom in and zoom out. It allows enlargement or reduction of images pressing the secondary mouse button and moving the cursor up (enlargement) or down (reduction). f) Colour. It is possible to customize the colour of the 3D model to maximize the contrast level of the brain structures. g) Transparency. Levels can be changed for each 3D model (see Figure 2).

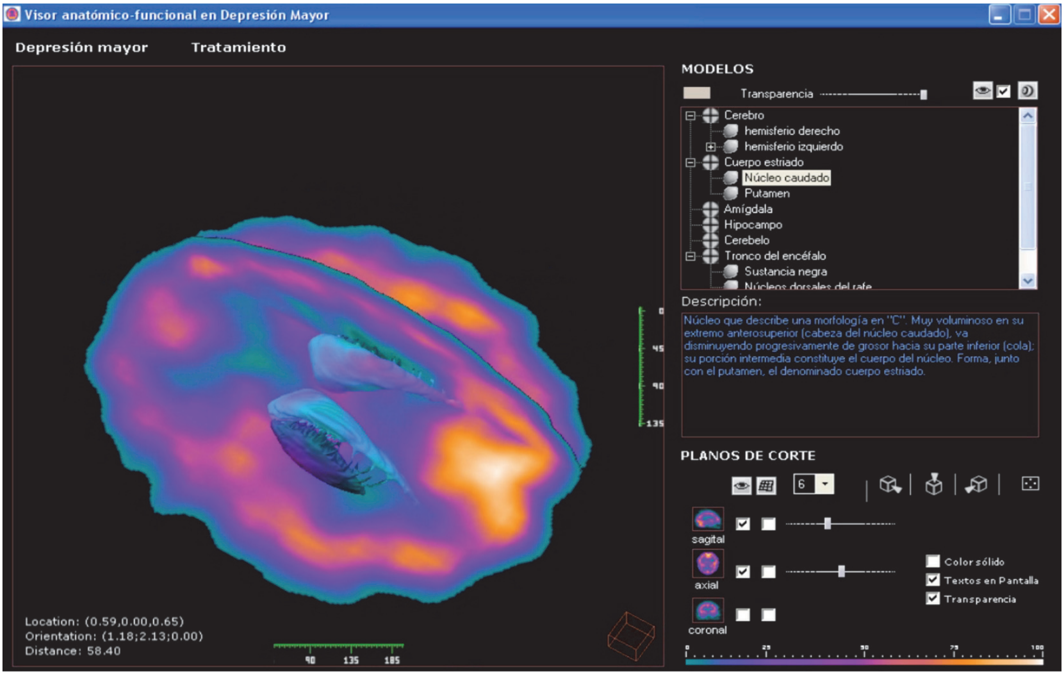

Figure 1: Anatomical and functional viewer of brain structures (left) and interactivity controls (right). (Note: Translation of the text (original in Spanish) from top to bottom and left to right: major depression; treatment; models; brain; right hemisphere; left hemisphere; corpus striatum; caudate nuclei; putamen nuclei; amgydala; hippocampus; cerebellum; brainstem; description; cut planes; solid colour; text in screen; transparency).

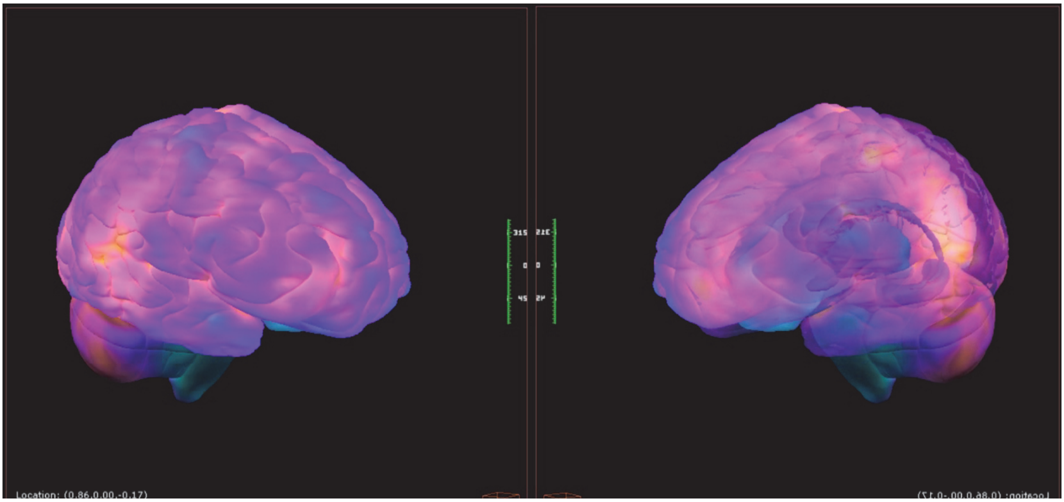

Figure 2: Changes in transparency for visualization of internal brain structures.

3.2. Visualization and Interactivity Features for Plane Cuts

The anatomical functional viewer interface allows the visualization of 3D embedded models (plane cuts) corresponding to SPECT sections (Figure 1). Specifically, three possible orthogonal planes can be independently activated clicking on them: sagittal plane (lateral), axial plane (hori–zontal) and coronal plane (frontal). The following interactivy features were included: a) Predefined views. An icon is located in the plane cut control area, which enables camera orientation in three predefined views (lateral right-left views and upper view). b) Plane position. A scrollbar allows each plane cut level to shift position by moving the cursor horizontally. c) Measurement. A grid icon was included for calculating relative distances between brain structures and functional SPECT sections. The grid quadrants are defined by the number of rows and columns, that can be changed using the numerical dropbox icon located in the control area (Figure 3).

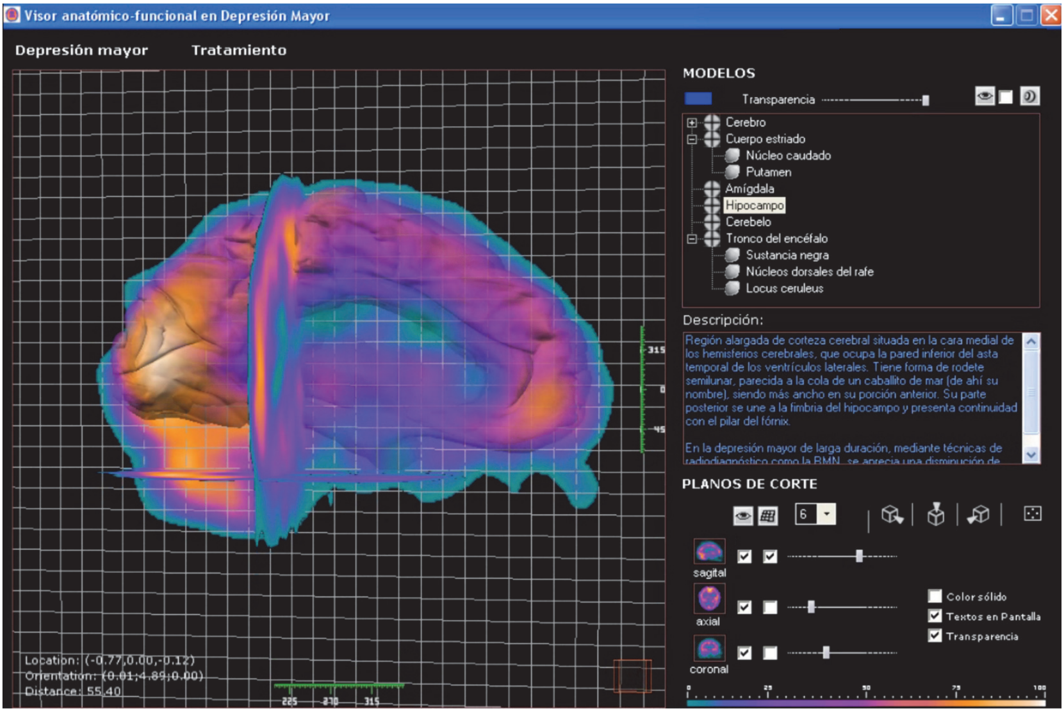

Figure 3: The grid feature for calculation of distances and sizes.

Additional visualization options include different multimedia contents. Animations that illustrate major depression characteristics and the current neurobiological mechanisms of typical pharma–cological treatments are included (Figure 4 *on following page*). Sound control and a line of reproduction, which allow moving and finding specific parts within the animation, were included. The visible areas on screen can also be captured and stored as a bitmap (.bmp extension).

3.3. Evaluation of Satisfaction and Perceived Usefulness

The students showed a high level of satisfaction with the tool in terms of visual attraction, inter–active capacity and content integration (M = 4.81, SD = 0.17). They also perceived a high usefulness for teaching purposes (M = 4.79; SD = 0.14).

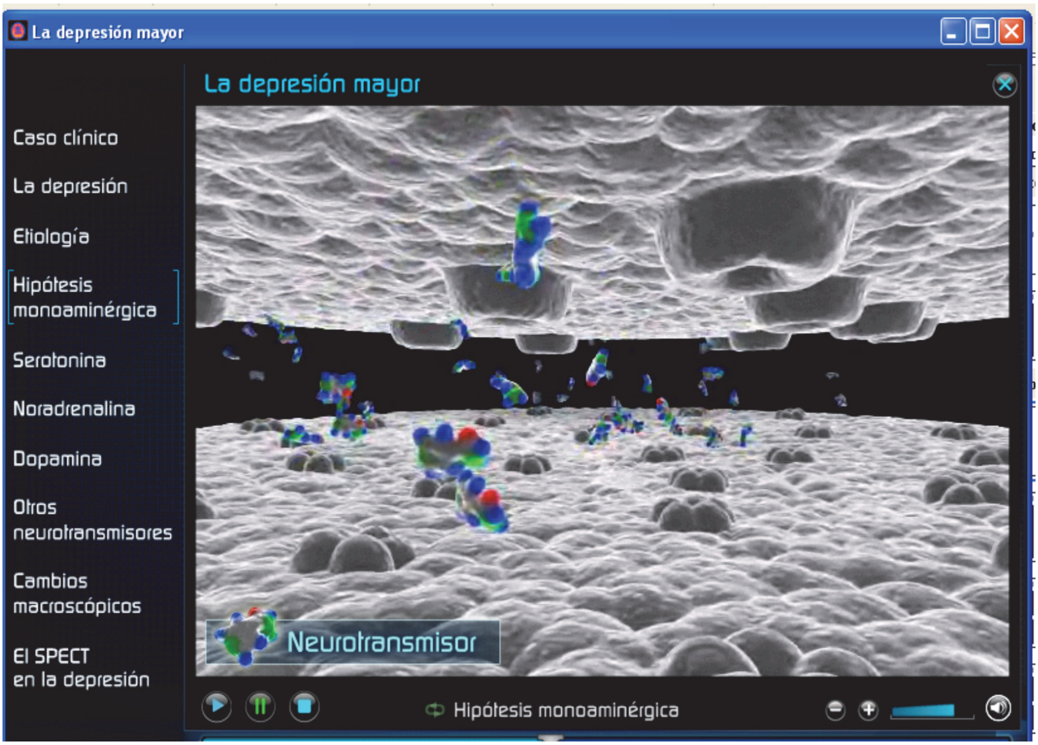

Figure 4: Representation of the monoaminergic mechanism underlying pharmacological treatment of depressive disorders (Note: Translation of the text (original in Spanish) from top to bottom: major depression; clinical case; about depression; etiology; monoaminergic hypothesis; serotonin; noradrenaline; dopamine; others neurotransmitters; macroscopic changes; SPECT in depression).

4. Discussion

This study illustrates an innovative ICT tool to facilitate the learning process related to the neurobiological basis of major depressive disorder. Digital 3D models embedded in real functional images provide a more comprehensive representation of single brain structures, and their relative spatial position, than those obtained from traditional cross-sectional images (e.g., atlases). Furthermore, the intuitive visual environment offers the opportunity of maximizing the user's independence and interactivity in the learning process, particularly when powerful multimedia elements (3D models, plus text, navigation controls, graphic elements) are combined in the same application.

To support the application of this tool, Ruisoto *et al* (2012) demonstrated that the use of 3D images increase the accuracy to locate brain structures in comparison with conventional cross-sectional exploration. Basically, this approach based on 3D visualization is supported by the fact that these models reduce cognitive demand associated with visual reconstruction of 2D cross-sectional images (Drake *et al*, 2009). This is a key goal in the study of neuroanatomy because learners have reported difficulties in understanding neuroanatomy with conventional 2D image exploration (Dev *et al*, 2002; Zinchuk *et al*, 2010), which require a high load of cognitive demand (Paas *et al*, 2003; Pass *et al*, 2004). Accordingly, Kirschner *et al* (2011) suggested that an appropriate instructional design would not only decrease cognitive overload, but increase the likehood of learners to be actively engaged in the learning tasks.

Student's satisfaction level was high. In this regard, Silén *et al* (2008) demonstrated that the possibility of rotating 3D visualizations was a suitable feature for neuroanatomy students. Moreover, Gould *et al* (2008) found that multimedia contents of the nervous system were perceived as highly useful by students of health sciences. Specifically, they found that the use of 3D images enhanced insights about the morphology and spatial relationship of the brain structures. Other issues such as the interactivity with the contents and its intuitive design should also be considered as explanatory factors of the high satisfaction reported by the students (Clark *et al*, 2006; Clark and Mayer, 2007).

Some limitations of the study should be outlined. Although this tool is a good approach to study the neurobiological basis of major depressive disorder, its use for clinical diagnosis is limited. In addition, the tool is only available in Spanish and limited to MicrosoftTM operating system, but the English translation and the adaptation to other operative systems (e.g., OS X, linux distributions, android and iOS) will be considered in the near future. Finally, preliminary data of satisfation was shown, but a more extensive scale to assess satisfaction is needed.

5. Conclusion

ICT tools are useful to understand the neurobiological mechanism associated with major depres–sive disorders. The integration of neuroanatomical structures and functional brain images with ICT tools facilitates the understanding of complex contents involved in the study of major depression. Overall, these applications open new possibilities of learning and knowledge access.

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Biographical Notes

Pablo Ruisoto Palomera *received a degree in Psychology and a PhD in clinical Neuropsychology from the University of Salamanca, Spain. He is currently a professor in the field of Psychobiology with a special interest in neuroscience and neuroanatomy in particular. His research interests include the development, appli–cation and evaluation of technological applications in neuroscience, specifically, their role in learning and teaching neuroanatomy. He is deeply inspired by new open source applications such as Osirix, Opensesame and Psychopy.*

Pablo Ruisoto Palomera

Juan A. Juanes Méndez *MD and PhD is professor with Tenure of Human Anatomy at the University of Salamanca. He also received a degree in Software Engineering from the Pontificia University of Salamanca. He is member of the Expert Panel for the National Agency for Evaluation and Accreditation of Health Sciences Professors. He is the leading researcher for Advanced Medical Visualization System Group at the University of Salamanca and has received 14 awards for his research and teaching. He has co-authored 19 academic books, published more than 100 articles and presented more than 300 communications in national and international congresses.*

Juan A. Juanes Méndez

María A. Velasco Marcos

María A. Velasco Marcos *received her MD and PhD from the University of Salamanca. She specializes in Primary and Community Care at the Elena Ginel Health Centre in Salamanca. Her training includes a degree in Family Advice and Orientation from the Pontificia University of Salamanca and Public Health from the National School of Health and Health Institute Carlos III. She has given numerous courses about communication and management of clinical depression in primary care. She has also published a number of research articles in peer-review journals and presented several communications in national and international congresses.*

Israel Contador Castillo

Israel Contador Castillo, *PhD is professor of Psychology at the Department of Basic Psychology, Psychobiology and Methodology of Behavioral Sciences, University of Salamanca, Spain. He is particularly interested in the neuropsychology field, and his research covers topics such as dementia, mild cognitive impairment and memory disorders. He is keen to contribute in developing innovative systems, which can help to understand the biological basis of human behaviour.*

Alberto Prats Galino

Alberto Prats Galino *MD and PhD is Department Head of Human Anatomy at the University of Barcelona and leading researcher for the group called Virtual Anatomy and Simulation at the Centre for Learning and Research Resources at the University of Barcelona, and responsible for the Quirurgical Neuroanatomy Unit in the Medical School at the University of Barcelona. He is currently responsible for numerous research and teaching innovation projects, and scientific committee member of several peer-review journals. He researches neuroimaging from a multi–disciplinary approach, integrating anatomy, radiology, nuclear medicine and bio–physics state-of-the-art research.*